JACC Vol. 16, No. 2
August 1990:304–10

Comparison of the Natural History of New Onset and Exacerbated Chronic Ischemic Heart Disease

LINDA D. WHITE, MD, MPH,*† THOMAS H. LEE, MD, FACC,*† E. FRANCIS COOK, ScD,*‡ MONICA C. WEISBERG, RN,* GREGORY W. ROUAN, MD,§ DONALD A. BRAND, PhD,|| LEE GOLDMAN, MD, FACC*† AND THE CHEST PAIN STUDY GROUP

Boston, Massachusetts; New Haven, Connecticut and Cincinnati, Ohio

To compare the natural history of patients with new onset ischemic heart disease with that of patients with exacerbations of chronic ischemic heart disease, short- and long-term outcomes of 3,465 emergency room patients with acute ischemic heart disease at four community and three university hospitals were evaluated. Acute myocardial infarction was diagnosed in 598 (33%) of the 1,835 patients with a prior history of infarction or angina and 934 (57%) of the 1,630 without such a history ($p < 0.001$). Patients with new onset ischemic heart disease with acute myocardial infarction were more likely than patients with infarction and exacerbated chronic ischemic heart disease to have Q wave infarction (57% versus 36%) and to receive thrombolytic therapy (11% versus 5%); they also had higher maximal creatine kinase levels (1,088 ± 1,299 versus 733 ± 906 U/liter) ($p < 0.0001$ for all three). After adjustment for differences in clinical presentation and initial triage, patients with new onset ischemic heart disease with acute myocardial infarction were less likely than the comparison group to have congestive complications (odds ratio 0.63, 95% confidence interval 0.47 to 0.84, $p < 0.01$) but not less likely to have arrhythmic, ischemic or overall complications. Among patients with angina without acute myocardial infarction, patients with new onset ischemic heart disease were less likely to have recurrent ischemic pain and congestive heart failure. In multivariate analysis of long-term follow-up data on 457 patients from one hospital, patients with new onset ischemic heart disease had better cardiovascular survival rates.

These data demonstrate that patients with new onset ischemic heart disease tend to have a better short- and long-term cardiovascular prognosis than do patients with exacerbated chronic ischemic heart disease.

(J Am Coll Cardiol 1990;16:304–10)

Patients with new onset angina are often included among those with the syndrome of unstable angina, a diagnostic category that also includes exacerbations of chronic angina, recurrence of stable angina and rest angina (1–9). However, some data indicate that new onset ischemic heart disease may represent a syndrome distinct from other types of acute ischemic heart disease. In angiographic studies (10,11), patients with new onset angina have had a higher prevalence of single vessel disease and a lower prevalence of three vessel and left main coronary artery disease than did patients with chronic angina. Nevertheless, long-term follow-up data suggest that patients with new onset angina are at increased risk of subsequent myocardial infarction or death compared with patients with chronic angina (10), and cardiac enzyme data indicate that patients with no history of ischemic heart disease who have acute myocardial infarction have a larger infarct than do patients with a history of ischemic heart disease (12).

These prior investigations were restricted to patients who had undergone coronary angiography (10,11) or were limited by small sample size (11,12). To gain insight into the natural history of these chest pain syndromes we compared the short- and long-term outcomes of patients seen in an emergency room with new onset ischemic heart disease or with worsening of chronic ischemic heart disease.

From *Brigham and Women's Hospital, †Harvard Medical School and the ‡Harvard School of Public Health, Boston, Massachusetts; §University of Cincinnati Hospital and University of Cincinnati, Cincinnati, Ohio and ||Yale-New Haven Hospital and Yale University School of Medicine, New Haven, Connecticut. The members of the Chest Pain Study Group and their affiliations are listed elsewhere (Reference 13). This study was supported in part by Grant 12543 from the Robert Wood Johnson Foundation, Princeton, New Jersey and Grant 83102-2H from the John A. Hartford Foundation, New York, New York. During the performance of this work, Dr. White was a fellow of the Charles A. Dana Foundation, New York. Dr. Lee is the recipient of a Public Health Service Clinical Investigator Award (HL01594-01) from the National Heart, Lung, and Blood Institute, Bethesda, Maryland. Dr. Rouan is a Teaching and Research Scholar of the American College of Physicians, Philadelphia, Pennsylvania, and was supported in part by a grant to the Training Program in Clinical Effectiveness from the W.K. Kellogg Foundation, Battle Creek, Michigan.

Manuscript received November 6, 1989; revised manuscript received February 7, 1990, accepted March 7, 1990.

Address for reprints: Thomas H. Lee, MD, Division of Clinical Epidemiology, Department of Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115.

0735-1097/90/$3.50

Methods

Study patients. The Multicenter Chest Pain Study is a cooperative investigation of the clinical characteristics and outcomes of emergency room patients with acute chest pain (13–22). All patients ≥30 years old who were seen in an emergency room with a chief complaint of anterior, precordial or left-side chest pain unexplained by obvious local trauma or abnormalities on chest roentgenogram were eligible for the study for up to three visits. This report includes data from a subset of the 12,140 patients who were enrolled from December 1983 to November 1986 at three university and four community hospitals. The institutions participating in the study and the date on which each center started entering patients are Brigham and Women's Hospital (January 1984); Yale-New Haven Hospital (December 1983); Danbury Hospital, Danbury, Connecticut (January 1984); Milford Hospital, Milford, Connecticut (June 1984); St. Mary's Hospital, Waterbury, Connecticut (April 1984); University of Cincinnati Hospital, Cincinnati, Ohio (July 1984) and William Beaumont Hospital, Royal Oak, Michigan (June 1985).

Emergency room protocol. Clinical data from the emergency room evaluation including history, physical examination, presence or absence of a prior electrocardiogram (ECG) and the emergency room ECG interpretation were recorded as part of a detailed protocol by the physician in the emergency room or by a research nurse. The person who completed the emergency room form had no knowledge of and thus could not be influenced by the patient's course after treatment in the emergency room. Follow-up data on subsequent complications and procedures experienced by the patient were recorded from the patient's hospital chart by research personnel who had no knowledge of the patient's initial emergency room status.

Admitted and nonadmitted patients. All admitted patients were included in the Chest Pain Study; nonadmitted patients were excluded if they did not consent to return in 48 to 72 h for measurement of cardiac enzymes and an ECG. All data were collected under protocols approved by institutional review boards. Nonadmitted patients who gave consent but would not return for follow-up evaluation were contacted by telephone to assess their clinical status. In such cases nonadmitted patients who were considered at higher risk for myocardial infarction because of a suggestive pain description, ECG abnormalities or continuing symptoms were encouraged by telephone to return for evaluation. Among consenting nonadmitted adults, 59% had follow-up visits and 45% had follow-up measurement of cardiac enzyme levels. Among patients who were unwilling to return, further follow-up was obtained by telephone and contact with the patient's personal physician. Nonadmitted patients were retained in the study only if the investigators, who did not know the patient's emergency room data, felt that follow-up information was sufficient to place the patient into one of the diagnostic categories. Overall, 85% of all potentially eligible patients were enrolled in the study and only 3.5% had insufficient follow-up data for assignment of diagnosis.

Exclusion and inclusion criteria. For the investigation of the natural history of new onset ischemic heart disease, eligible subjects included patients in the Multicenter Chest Pain Study who received a final diagnosis of myocardial infarction or angina. Patients were excluded if their final diagnosis was noncardiac chest pain (7,701 patients), if they had a history of angina but did not describe their current symptoms as worse than their previous angina (274 patients), if they had a history of myocardial infarction but did not describe their current symptoms as similar to those of a prior infarction or worse than previous angina (548 patients) or if information comparing their current and previous angina was unavailable (152 patients). The 3,465 remaining patients included 1,630 patients who denied any history of myocardial infarction or angina (new onset disease) and 1,835 patients with a history of myocardial infarction or angina who described their current chest pain as worse than their chronic angina or similar to that associated with a prior infarction (exacerbated chronic disease).

Follow-up. Survival status at ≥1 year was determined for the subset of 457 patients who were evaluated in the Brigham and Women's Hospital emergency room and were discharged from either the hospital or the emergency room; 166 patients had new onset ischemic heart disease and 291 had exacerbated chronic disease. Follow-up information was obtained from the patient, relatives or medical records for 433 patients (95%) and from the Massachusetts Bureau of Vital Statistics for the other 24 (5%). Mean follow-up times for the new onset and exacerbated chronic groups were 2.4 ± 0.8 and 2.3 ± 0.9 years, respectively.

Definition of outcomes. *Acute myocardial infarction.* This was diagnosed if one of the following criteria was met within 1 week of the emergency room evaluation: 1) characteristic evolution of serum enzyme levels including myocardial creatine kinase (MB CK) isoenzyme detected in more than trace amounts by qualitative electrophoretic assay or in amounts of at least 5% of the total CK level with a typical rise and fall by quantitative assays; or, if MB CK was not assayed, a typical rise and fall of the total CK level with a peak value at least twice the upper limit of normal; or a lactate dehydrogenase (LDH) isoenzyme-1 level greater than the isoenzyme-2 level in the absence of hemolysis or renal infarction; 2) ECGs showing development of new pathologic Q waves (≥0.04 s in duration) and ≥25% decrease in the amplitude of the following R wave compared with that of the emergency room ECG; or 3) scintigraphic scans showing focal uptake of technetium-99m stannous pyrophosphate in the cardiac area if the serum enzyme peak occurred before

hospitalization and if the patient had no history of myocardial infarction or valvular calcification.

Patients who had sudden death or cardiac arrest. In addition, because the purpose of the Chest Pain Study is to define optimal management strategies for patients with acute chest pain, patients with sudden death within 72 h of their emergency room evaluations were classified as having infarction unless there were contradictory data. Patients who had a sudden in-hospital cardiac arrest were also classified as having acute myocardial infarction if they died before it was possible to obtain enzymatic confirmation of myocardial necrosis and if there were no other explanations for the arrest. In all such patients the presenting characteristics, ECG and clinical course were most consistent with acute myocardial infarction.

Unstable angina. This was diagnosed if the patient's original emergency room chest pain syndrome was either new or worse (in frequency, severity or duration) than his or her chronic anginal syndrome and if the diagnosis of angina was made by the senior clinician involved with the case.

Acute ischemic heart disease. Patients were classified as having acute ischemic heart disease if they received a final diagnosis of either myocardial infarction or unstable angina. Final diagnoses were made during hospitalization if the patient was admitted and at time of follow-up if the patient was not admitted to the hospital.

Short-term outcome, complications and procedures. The short-term outcomes of interest included death, major complications and major procedures occurring within 72 h of presentation. Major complications were grouped as arrhythmic (ventricular fibrillation, new complete heart block, cardiac arrest, new Mobitz type II heart block, atrioventricular dissociation), ischemic (infarct extension, recurrent ischemic pain) and congestive (congestive heart failure, pulmonary edema, cardiogenic shock). Procedures included emergency cardioversion, intubation other than during a surgical procedure, intraaortic balloon pump, temporary pacing, pulmonary artery catheterization and cardiac catheterization followed by coronary artery bypass grafting on the same admission.

Statistical methods. Patients were divided into subpopulations by final diagnosis (acute myocardial infarction versus angina without infarction) for all analyses. Differences in clinical presentations and triage decisions between the groups with new onset and exacerbated chronic disease were evaluated with chi-square tests of association for categoric variables and Wilcoxon midrank tests for continuous variables. Analysis of short-term complication rates was performed using logistic regression analysis (23) to evaluate the effect of new onset ischemic heart disease on complication rates.

In addition to history of angina, variables were included in the regression models to adjust for the following clinical and triage characteristics: age, gender, time since onset of pain (<4 h), location of pain (substernal or other), pain quality (pressure or other), pain radiation to the arms, shoulders, neck, jaw or face; associated diaphoresis, reproduction of pain by chest wall palpation, deep breathing or changes in position, presence or absence of rales, presence of ischemic changes on the emergency room ECG and admission to a coronary care unit. For patients with acute myocardial infarction other variables that were added to the regression models included infarct location, presence of pathologic Q waves, maximal creatine kinase level and use of thrombolytic therapy.

Long-term survival was measured in terms of death from cardiac causes and death from all causes. The long-term survival rates of patients with new onset ischemic heart disease and patients with worsened, chronic ischemic heart disease were compared using the log rank test and Cox regression analysis (24). After adjustment for the clinical and triage features entered in the logistic regression models, the inclusion of infarct location, presence of pathologic Q waves, maximal creatine kinase level and use of thrombolytic therapy did not alter the relation between new onset angina (versus exacerbated chronic angina) and long-term survival among patients with acute myocardial infarction. Therefore, to enhance statistical efficiency, these four features that are pertinent only to patients with an acute myocardial infarction were eliminated from the long-term survival analysis and all patients were fitted to a single model containing the other listed features and an added term for the presence of an acute myocardial infarction.

Results

Clinical characteristics. Acute myocardial infarction was diagnosed in 934 (57%) of the 1,630 patients with new onset ischemic heart disease and 598 (33%) of the 1,835 patients with exacerbation of chronic ischemic heart disease ($p < 0.001$). The groups with exacerbated chronic or new onset ischemic heart disease differed in several presenting clinical characteristics (Table 1). Among the 1,532 patients with acute myocardial infarction, those with new onset disease were significantly younger, less likely to describe the quality of their pain as "pressure" or to have bibasilar rales and they were more likely to have changes of ischemia or infarction not known to be old on the emergency room ECG. Among the 1,933 patients with angina without infarction, patients with new onset disease were younger and less likely to describe the quality of their pain as "pressure" or to have bibasilar rales.

The evaluating physicians were more likely to admit patients with acute myocardial infarction to the hospital if they had a history of ischemic heart disease (98% versus 95%, $p < 0.001$) (Table 2). Similarly, patients with angina without infarction were more likely to be admitted to the

Table 1. Clinical Characteristics of 3,465 Patients With Acute Ischemic Heart Disease

	Acute Myocardial Infarction			Angina Without Infarction		
	Ischemic Heart Disease Pattern			Ischemic Heart Disease Pattern		
	Exacerbated Chronic (n = 598)	New Onset (n = 934)	p Value	Exacerbated Chronic (n = 1,237)	New Onset (n = 696)	p Value
Mean age ± SD (yr)	65.6 ± 12.5	60.8 ± 13.2	<0.001	65.2 ± 12.1	60.9 ± 12.1	<0.0001
Male gender	379 (63%)	614 (66%)	NS	645 (52%)	379 (54%)	NS
Time since onset of pain ≤4 h	357 (61%)	509 (56%)	NS	644 (53%)	332 (49%)	NS
Pain mainly substernal	510 (85%)	818 (88%)	NS	993 (80%)	579 (83%)	NS
Pain quality pressure	434 (74%)	567 (62%)	<0.001	862 (71%)	425 (63%)	<0.001
Radiation of pain to jaw, neck, left arm or left shoulder	291 (49%)	459 (49%)	NS	592 (48%)	301 (43%)	0.05
Diaphoresis	318 (53%)	485 (52%)	NS	460 (37%)	275 (40%)	NS
Pain reproduced by deep breathing	22 (4%)	42 (5%)	NS	45 (4%)	33 (5%)	NS
Rales ≥bibasilar	189 (32%)	188 (20%)	<0.001	281 (23%)	75 (11%)	<0.001
Emergency room ECG changes of ischemia or infarction	404 (73%)	706 (81%)	<0.001	442 (40%)	236 (37%)	NS

ECG = electrocardiogram; NS = p value >0.05. For patients with a diagnosis of acute myocardial infarction, data were missing for time since onset of pain for 8 patients with new onset and 22 patients with exacerbated chronic ischemic heart disease; for quality of chest pain for 10 patients with new onset and 15 patients with exacerbated chronic ischemic disease; and for emergency room ECG interpretation for 48 patients with new onset and 65 patients with exacerbated chronic disease. For patients with a diagnosis of angina without infarction, data were missing for time since onset of pain for 23 patients with new onset and 24 patients with exacerbated chronic disease; for quality of chest pain for 18 patients with new onset and 17 patients with exacerbated chronic disease; and for emergency room ECG interpretation for 126 patients with new onset and 57 patients with exacerbated chronic disease.

hospital or to the coronary care unit if they had such a history.

Clinical Outcomes

Patients with acute myocardial infarction. Among the 1,532 patients with acute myocardial infarction, patients with new onset ischemic heart disease had higher peak creatine kinase levels (1,088 ± 1,299 versus 733 ± 906 U/liter, $p < 0.0001$), were more likely to have Q wave infarction (57% versus 36%, $p < 0.0001$) and were more likely to receive thrombolytic therapy (11% versus 5%, $p < 0.0001$) than were patients with exacerbated chronic disease.

Table 2. Initial Triage Decisions for 3,465 Patients With Acute Ischemic Heart Disease

	Acute Ischemic Heart Disease Pattern		
	Exacerbated Chronic	New Onset	p Value
Final diagnosis: acute myocardial infarction	(n = 598)	(n = 934)	
Admitted to hospital	588 (98%)	889 (95%)	<0.001
Admitted to ICU/CCU	554 (93%)	843 (90%)	NS
Final diagnosis: angina without infarction	(n = 1,237)	(n = 696)	
Admitted to hospital	1,207 (98%)	633 (91%)	<0.001
Admitted to ICU/CCU	975 (79%)	469 (67%)	<0.001

ICU/CCU = intensive or coronary care units.

The location of the infarct was anterior for 300 patients (32%) with new onset ischemic heart disease and 170 patients (28%) with exacerbated chronic disease (p = NS).

Patients with new onset ischemic heart disease were less likely to die in the hospital (5% versus 9%, $p < 0.01$) and less likely to have complications of congestive heart failure (15% versus 20%, $p < 0.05$) or pulmonary edema (3% versus 7%, $p < 0.001$) (Table 3). The two groups had similar overall procedure rates, but patients with exacerbated chronic disease more often underwent cardiac catheterization followed by coronary artery bypass grafting during the same admission.

When logistic regression analysis was used to adjust for differences in clinical and triage features, patients with myocardial infarction and new onset ischemic heart disease were less likely to have congestive complications (congestive heart failure, pulmonary edema or cardiogenic shock) than were patients with exacerbated chronic disease (odds ratio 0.63, 95% confidence interval 0.47 to 0.84, $p < 0.01$). However, in this adjusted analysis, no differences in the rates of arrhythmic, ischemic and overall complications or major procedures were detected.

Patients with angina without acute myocardial infarction. The in-hospital mortality rate was low among the 1,933 patients diagnosed as having angina without infarction whether or not they had a history of ischemic heart disease (Table 3). The rate of complications in the first 72 h was lower in the 696 patients with new onset angina than in the 1,237 patients with exacerbated chronic disease (28% versus

Table 3. Clinical Outcome During First 72 h in 3,465 Patients With Acute Ischemic Heart Disease

Outcome	Acute Myocardial Infarction			Angina Without Infarction		
	Ischemic Heart Disease Pattern			Ischemic Heart Disease Pattern		
	Exacerbated Chronic (n = 598)	New Onset (n = 934)	p Value	Exacerbated Chronic (n = 1,237)	New Onset (n = 696)	p Value
Death in hospital	51 (9%)	47 (5%)	<0.01	3 (0.2%)	2 (0.3%)	NS
≥1 Complication	402 (67%)	575 (62%)	<0.05	444 (36%)	194 (28%)	<0.001
≥1 Arrhythmic complication	74 (12%)	110 (12%)	NS	8 (0.7%)	3 (0.4%)	NS
Ventricular fibrillation	17 (3%)	29 (3%)	NS	4 (0.3%)	3 (0.4%)	NS
Complete heart block	13 (2%)	39 (4%)	<0.05	1 (0.1%)	1 (0.1%)	NS
Cardiac arrest	55 (9%)	51 (5%)	<0.01	4 (0.3%)	2 (0.3%)	NS
Mobitz type II heart block	1 (0.2%)	9 (1%)	NS	0 (0%)	0 (0%)	—
Atrioventricular dissociation	13 (2%)	6 (1%)	<0.01	1 (0.1%)	0 (0%)	NS
≥1 Ischemic complication	311 (52%)	457 (49%)	NS	390 (32%)	177 (25%)	<0.01
Infarct extension	12 (2%)	30 (3%)	NS	0 (0%)	0 (0%)	—
Recurrent ischemic pain	308 (52%)	452 (49%)	NS	390 (32%)	177 (25%)	<0.01
≥1 Congestive complication	180 (30%)	194 (21%)	<0.001	93 (8%)	32 (5%)	<0.05
Congestive heart failure	116 (20%)	137 (15%)	<0.05	74 (6%)	25 (4%)	<0.05
Pulmonary edema	44 (7%)	27 (3%)	<0.001	17 (1%)	6 (1%)	NS
Cardiogenic shock	46 (8%)	56 (6%)	NS	6 (0.5%)	2 (0.3%)	NS
≥1 Major procedure	155 (26%)	233 (25%)	NS	72 (6%)	22 (3%)	<0.01
Cardioversion	31 (5%)	40 (4%)	NS	9 (0.7%)	3 (0.4%)	NS
Intubation	49 (8%)	59 (6%)	NS	6 (0.5%)	2 (0.3%)	NS
Intraaortic balloon pump	34 (6%)	45 (5%)	NS	12 (1%)	6 (1%)	NS
Temporary pacing	49 (8%)	68 (7%)	NS	5 (0.4%)	3 (0.4%)	NS
Pulmonary artery catheter	93 (16%)	168 (18%)	NS	22 (2%)	12 (2%)	NS
Cardiac catheterization leading to surgery	24 (4%)	18 (2%)	<0.05	43 (3%)	10 (1%)	<0.01

36%, $p < 0.001$). This difference was mostly due to a decreased incidence of recurrent ischemic chest pain and congestive heart failure among patients with new onset angina. Patients with new onset angina also had significantly lower rates of major procedures because they were less likely to have cardiac catheterization followed by coronary artery bypass grafting on the same admission.

In multivariate analyses, among patients without infarction, those with new onset angina did not differ significantly from patients with exacerbated chronic angina in overall risk of complications. However, in the adjusted analysis the patients with new onset angina still had a significantly lower major procedure rate (odds ratio 0.51, 95% confidence interval 0.30 to 0.88).

Posthospitalization Survival

During follow-up (mean 2.3 ± 0.8 years) of 458 patients who were discharged from Brigham and Women's Hospital, there were a total of 78 deaths including 53 from cardiac causes. Among patients with acute myocardial infarction, there were 16 deaths (13 cardiac) among the 75 patients with exacerbated chronic ischemic heart disease and 13 deaths (10 cardiac) among the 96 patients with new onset ischemic heart disease. Among patients without acute myocardial infarction, there were 40 deaths (27 cardiac) among the 216 patients with exacerbated chronic ischemic heart disease and 9 deaths (3 cardiac) among the 71 patients with new onset angina.

Life table analyses revealed a nonstatistically significant trend ($p = 0.09$) toward better overall posthospitalization survival of patients with new onset acute ischemic heart disease than among patients with exacerbated chronic ischemic heart disease. Survival rates at 1, 2 and 3 years were 93%, 90% and 85%, respectively, among patients with new onset disease and 91%, 83% and 81%, respectively, among patients with exacerbated chronic ischemic heart disease.

However, postdischarge cardiovascular survival was significantly better in patients with new onset ischemic heart disease ($p < 0.05$). Cardiovascular survival rates at 1, 2 and 3 years were 95%, 94% and 91%, respectively, in this group and 93%, 88% and 86%, respectively, among patients with exacerbated chronic ischemic heart disease.

When multivariate Cox regression models were used to adjust for other clinical data (see Methods), patients with new onset ischemic heart disease were found to have a better cardiovascular prognosis than did patients with exacerbated chronic disease. These multivariate analyses indicated that

the relative risk of cardiac death associated with new onset ischemic heart disease was 0.47 (95% confidence interval 0.23 to 0.97); the relative risk of all deaths was 0.74 (95% confidence interval 0.42 to 1.29).

Discussion

New onset versus exacerbated chronic ischemic heart disease. This study of 3,465 emergency room patients demonstrates that patients with new onset ischemic heart disease tend to have a better cardiovascular prognosis than patients with exacerbated chronic ischemic heart disease. The difference in short-term prognosis was particularly apparent in cases of acute myocardial infarction where patients with a history of ischemic heart disease had higher predischarge mortality and rate of congestive complications. These data demonstrate that although the size of the infarct may be smaller among patients with a history of coronary heart disease (12), the infarct may lead to heart failure and death when imposed on a left ventricle that has been previously damaged.

Recurrent angina in patients with a prior history of coronary disease. Similarly, patients who had angina but not infarction were more likely to have complications such as recurrent ischemic pain or congestive heart failure if they had a history of coronary heart disease. These patients were also more likely to undergo coronary angiography followed by coronary artery bypass graft surgery during their admission. This increased use of procedures may indicate that exacerbations of chronic ischemic heart disease were occurring despite an antianginal regimen in most cases.

Long-term follow-up. The better cardiovascular prognosis of patients with new onset ischemic heart disease was also reflected in the analysis of long-term follow-up data. However, this analysis could not adjust for findings that resulted or might have resulted from the performance of specialized tests for prognostic stratification such as exercise testing, echocardiography or coronary angiography. Information from further testing might eliminate the independent correlation of a history of ischemic heart disease with postdischarge mortality.

Acute infarction versus angina as first manifestation of ischemic heart disease. The rate of acute myocardial infarction in the 1,630 patients with new onset ischemic heart disease in our study group was nearly twice that of patients with exacerbations of chronic ischemic heart disease (57% versus 33%, $p < 0.001$). This difference may reflect the difficulty of making the diagnosis of angina without infarction in patients without a history of ischemic heart disease or a lower threshold for diagnosing unstable angina in patients with a history of angina. In the absence of a gold standard for the diagnosis of angina without infarction, these data should not be interpreted as evidence that the first manifestation of ischemic heart disease is more likely to be acute myocardial infarction than angina.

This study adds to previous investigations of the natural history of ischemic heart disease syndromes by focusing on a large number of patients who had chest pain that was sufficiently acute to precipitate an emergency room visit and by performing multivariate analyses of the relations between a history of ischemic heart disease and subsequent clinical outcomes. Other investigators have studied smaller numbers of patients from more selected populations such as patients who were referred for and underwent coronary angiography (10), patients with acute myocardial infarction (12), hospitalized patients (6) or patients who were referred to special ambulatory clinics (25).

Conclusions. These data demonstrate that patients with new onset ischemic heart disease tend to have a better short- and long-term cardiovascular prognosis than do patients with exacerbated chronic ischemic heart disease. Nevertheless, both groups had an in-hospital mortality rate of <0.3% and a low rate of life-threatening complications in the absence of acute myocardial infarction. Thus, our data suggest that both groups of patients are appropriate for management in intermediate care settings rather than coronary care units when the probability of acute ischemia is too high for discharge to be safe (5) but the probability of acute myocardial infarction is low (13).

References

1. Braunwald E. Unstable angina: a classification. Circulation 1989;80: 410–4.
2. Fulton M, Duncan B, Lutz W, et al. Natural history of unstable angina. Lancet 1972;1:860–5.
3. Maseri A. Pathogenic classifications of unstable angina as a guideline to individual patient management and prognosis. Am J Cardiol 1986;80(suppl 4C):48–55.
4. Mulcahy R, Daly L, Graham I, et al. Unstable angina: natural history and determinants of prognosis. Am J Cardiol 1981;48:525–8.
5. Pozen MW, D'Agostino RB, Selker HP, Sytkowski PA, Hood WB. A predictive instrument to improve coronary-care-unit admission practices in acute ischemic heart disease. N Engl J Med 1984;310:1273–8.
6. Quale J, Kimmelstein C, Schrem S, Lipschik G, Stavens C. Identification of risk factors for development of acute myocardial infarction or life-threatening ventricular arrhythmia in unstable angina pectoris. Am J Cardiol 1987;59:703–4.
7. Quale J, Kimmelstein C, Lipschik G, Schrem S. Use of sequential cardiac enzyme analysis in stratification of risk for myocardial infarction in patients with unstable angina. Arch Intern Med 1988;148:1277–9.
8. Unstable Angina Pectoris Study Group: Unstable angina pectoris national cooperative study to compare medical and surgical therapy. I. Report of protocol and patient population. Am J Cardiol 1976;37:896–902.
9. Unstable Angina Pectoris Study Group: Unstable angina pectoris national cooperative study to compare medical and surgical therapy. II. In-hospital experience and initial follow-up results in patients with one, two, and three vessel disease. Am J Cardiol 1978;42:839–48.
10. Roberts KB, Califf RM, Harrell FE, Lee KL, Pryor DB, Rosati RA. The prognosis for patients with new-onset angina who have undergone cardiac catheterization. Circulation 1983;68:970–8.

11. Victor MF, Likoff MJ, Mintz GS, Likoff W. Unstable angina pectoris of new onset: a prospective clinical and arteriographic study of 75 patients. Am J Cardiol 1981;47:229–32.

12. Brush JE, Brand DA, Acampora D, Goldman L, Cabin HS. Relation of peak creatine kinase during acute myocardial infarction to presence or absence of previous manifestations of myocardial ischemia (angina pectoris or healed myocardial infarction). Am J Cardiol 1988;62:534–7.

13. Goldman L, Cook EF, Brand DA, et al. A computer protocol to predict myocardial infarction in emergency department patients with chest pain. N Engl J Med 1988;318:797–802.

14. Lee TH, Rouan G, Weisberg MC, et al. Clinical characteristics and natural history of patients with acute myocardial infarction sent home from the emergency room. Am J Cardiol 1987;60:219–24.

15. Lee TH, Cook EF, Weisberg MC, Sargent RK, Wilson C, Goldman L. Acute chest pain in the emergency room: identification and examination of low-risk patients. Arch Intern Med 1985;145:65–9.

16. Lee TH, Rouan GW, Weisberg MC, et al. Sensitivity of routine clinical criteria for diagnosing myocardial infarction within 24 hours of hospitalization. Ann Intern Med 1987;106:181–6.

17. Lee TH, Weisberg M, Cook EF, Daley K, Brand DA, Goldman L. Evaluation of creatine kinase and creatine kinase-MB for diagnosing myocardial infarction. Clinical impact in the emergency room. Arch Intern Med 1987;147:115–21.

18. Lee TH, Cook EF, Weisberg MC, Brand DA, Rouan GW, Goldman L. Candidates for thrombolysis among emergency department patients with acute chest pain: the Multicenter Chest Pain Study Experience. Ann Intern Med 1989;110:957–62.

19. Solomon CG, Lee TH, Cook EF, et al. Comparison of clinical presentation of acute myocardial infarction in patients older than 65 years of age to younger patients: the Multicenter Chest Pain Experience. Am J Cardiol 1989;63:772–6.

20. Beamer AD, Lee TH, Cook EF, et al. Diagnostic implications of the circadian variation of the onset of chest pain. Am J Cardiol 1987;60:998–1002.

21. Cunningham MA, Lee TH, Cook EF, et al. The effect of gender on the probability of myocardial infarction among emergency department patients with acute chest pain. J Gen Intern Med 1989;4:392–8.

22. Lee TH, Short LE, Weisberg MC, et al. Patients with acute chest pain who leave emergency departments against medical advice. J Gen Intern Med 1988;3:21–4.

23. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic Research: Principles and Quantitative Methods. New York: Van Nostrand Reinhold, 1982.

24. Kalbfleisch JD, Prentice RL. The Statistical Analysis of Failure Time Data. New York: John Wiley, 1980.

25. Duncan B, Fulton M, Morrison SL, et al. Prognosis of new and worsening angina pectoris. Br Med J 1976;1:981–5.